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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,688	11/06/2006	Makoto Suematsu	K2100.0001	7334

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DICKSTEIN SHAPIRO LLP
1177 AVENUE OF THE AMERICAS (6TH AVENUE)
NEW YORK, NY 10036-2714

EXAMINER	
NOBLE, MARCIA STEPHENS	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,688	SUEMATSU ET AL.	
	Examiner	Art Unit	
	MARCIA S. NOBLE	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *22-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/20/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-27 are pending. Claims 5, 11, 17, and 18 are amended by the amendment filed 7/20/2006.

Election/Restrictions

2. Applicant's election without traverse of Group I, claims 1-21, in the reply filed on 7/28/2008 is acknowledged.

Claims 22-27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/28/2008.

Claims 1-21 are under consideration.

Claim Rejections - 35 USC § 112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A carrier comprising a non-cationic surface that accumulates on an endothelial cell site of damaged tissue;

A pharmaceutical composition comprising a carrier comprising a non-cationic surface that accumulates on an endothelial cell site of damaged tissue, wherein the carrier also comprises a drug; and

A drug delivery method comprising administering the pharmaceutical composition (disclosed above) to an endothelial cell site of tissue damage in a subject, wherein the composition accumulates at said site and wherein the drug of said composition acts on the site of tissue damage.

The specification does not reasonably provide enablement for 1) a carrier that accumulates on a damaged tissues site that does not expose or comprise endothelial cells; and 2) a method that does not administer the carrier to a site of tissue damage. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make or use the claimed invention, if not, whether an artisan would require undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of

working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue".

1) The breadth of the instant claims encompasses a carrier that accumulates on a damaged tissues site that does not expose or comprise endothelial cells. However, the specification discloses, "A tissue for accumulating the carrier of the invention is not particularly limited as long as it comprises endothelial cells." (See p. 15, lines 7-8 of the specification.) The specification also discloses, "The carrier of the invention does not accumulate on an undamaged blood vessel and instead specifically accumulates on an endothelial cell sites damaged as described above." (See p. 15, lines 13-15 of the specification). Therefore, the specification discloses that invention at the very least must comprise the limitation of an endothelial cell site of damage because the carrier only accumulates on endothelial cell sites. The claims more broadly encompass a site of damage that does not comprise an endothelial cell site. However, the specification guidance provided by the specification suggests that the instant invention would not function with a site of damage that does not comprise endothelial cells because accumulation of the carrier on endothelial cells is the mechanism by which the instant invention functions. Therefore, because the instant carrier specifically functions by accumulation on endothelial cells, as taught by the specification, the specification does not enable the use of the instant carrier with a site of damage that does not comprise endothelial cells, as is embraced by the claims.

2) The methods of claims 17 to 21 encompass a drug delivery method that does not have the active step of administering the carrier comprising a drug to a subject. It is

well established in the art for a drug to be delivered to a site of tissue damage it must be administered to a site of tissue damage. The teachings of the specification clearly teach that the instant invention is meant to treat sites of tissue damage and individuals (p. 1, line 12 to p. 2, line 21). However, the claims do not require administering the carrier. Therefore, for the claimed method to be enabled by the specification, the instant claims required an active administration step because the invention would not function without such an administration step.

Overall, the instant claims embrace carriers and methods of using such carrier in a way that is not enabled by the specification. The specification clearly teaches that the carrier functions by accumulation on endothelial cells. However, the breadth of the claims encompasses a site of tissue damage without endothelial cells present. The breadth of the claims also encompasses a drug delivery method that does not administer the drug carrier. From the specification and teachings well established in the art, clearly these embodiments would not function. Therefore, these embodiments are not enabled by the specification. Therefore the instant claims are only enabled for the embodiments disclosed above.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 15 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 recites, "the drug is at least one selected from a group consisting of substances that are...uptake of an inflammation-mediated cell or enzyme degradation...". This recitation is indefinite because "uptake of an inflammation-mediated cell or enzyme degradations" are processes, not drugs or substances that would be considered drugs.

Claim 16 depends from claim 15.

Claim Objections

5. Claims 11-21 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 11 recites a drug transporter comprising the carrier of claim 1. The instant claim is not further limiting because the product does not comprise any structural limitations that are different than the carrier of claim 1. It is acknowledged that the preamble identifies the product as a drug transporter. However, the claim does not require the presence of a drug and structure of the product is the same as claim 1. Therefore, claim 11 is not further limiting to claim 1.

Claim 12-21 depend from claim 11.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-12 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Debs et al (US Patent No. 5,641,662, date of patent: 6/24/1997)

Debs et al discloses a non-cationic liposome used for gene therapy (col 17, lines 53-55). Debs et al discloses that the non-cationic liposome can be made of dioleoylphosphatidylcholine or phosphatidylethanolamine (col 17, lines 60-64), which are the same materials disclosed in the specification of the instant application to make the non-cationic carrier of the instant claims (see p. 9, line 11). Furthermore, because the instant carrier comprises all the same structural requirements as disclosed in Debs et al, inherently the carrier disclosed by Deb et al can be used for accumulation on a damaged vessel or damage associated with the various claimed diseases for claims 1-11. Therefore, Debs et al overall discloses all the limitation of the carrier of claims 1-11. Debs et al discloses that the non-cationic liposome is used to deliver nucleic acids to the lung for treatment of lung diseases (col 10, lines 27-29). Debs et al more specifically disclose nucleic acids to treat cancer (col 10, lines 60-62). Therefore, because Debs et al discloses non-cationic lipsomes carrying therapeutic nucleic acids, Debs et al discloses the claimed drug transporter and pharmaceutical composition, as claimed in claim 12. Furthermore, because Deb et al more specifically discloses anti-cancer nucleic acids, Debs et al discloses antitumor agents, as claimed in claim 15.

"Where, as here, the claimed and prior art products are identical or substantially

identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product (*In re Ludtke*). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972))." "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." See also MPEP 2113.

In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934) and MPEP 2112.01.

7. Claims 1-15 and 17-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Kazuo et al (JP 07-089874 (publication date: 4/04/1995; abstract is of record in the

IDS, filed 7/20/2006; translation p. 1-23 provided by STIC translation), as evidenced by Dictionary.com (http://dictionary.reference.com/browse/tinge).

Kazuo et al discloses a drug carrier tinged with positive charges in its surface that recognizes a blood vessel endothelium damage (p. 4, [0013], lines 1 to p. 5, line 2). According the Dictionary.com., the definition of "tinge" is "a slight admixture, as of some qualifying property or characteristic; trace; smattering" (see page 1 of Dictionary.com printout, definition # 4). Therefore, Kazuo et al discloses a drug carrier with only trace amount of positive charge on its surface which would not affect the overall neutral or anion charge. Therefore, Kazuo et al inherently discloses a non-cationic surface drug carrier as claimed, as evidenced by Dictionary.com. Furthermore, Kazuo et al discloses that the carrier can be made with such phospholipids as phosphatidylcholine, phosphatidylglycerol, and phosphatidylethanolamine (p. 6, [0036], line 1 to p. 7, line 3). These are the same material disclosed by specification for the production of the claimed carrier (See page 9, lines 5-22). Because Kazuo et al and the specification disclose carrier that are made of the same structural components, inherently the carriers of the instant claims and the carrier disclosed by Kazuo et al are the same. Also because the instantly claimed carrier and the carrier disclosed by Kazuo et al are the same, the carrier disclosed by Kazuo et al inherently has all the same functional properties and can be used for all the disclosed used in claims 1-10.

"Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently

possess the characteristics of his claimed product (*In re Ludtke*). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972))." "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." See also MPEP 2113.

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Katzuo et al disclose the drug carrier can be used anti-inflammatory agents, anticancer agents, angiotensin conversion enzyme inhibitor, agents that inhibit smooth muscle cell mobilization, platelet aggregating repressors, and overall inhibitors of thrombolysis (p. 5, [0025], lines 1-6). Therefore, Katzuo et al discloses the limitations of drug transporter and pharmaceutical composition of claims 11-15.

Katzuo et al discloses that the liposome of their invention is administered intravenously to rats comprising blood vessel damage and liposome accumulation was monitored (p. 13, [0091], line 1 to [0092], line 6). Katzuo et al discloses that the liposome accumulated in the endothelial site of blood vessel damage (p. 13, [0096], line 4 to p. 14, line 1). Katzuo discloses the use of the liposome to deliver drugs that depress blood vessel thickening in a site of endothelial cell damage (p. 15, [0113], lines 1-4). Katzuo discloses that the liposome successfully delivered said drugs and blood vessel thickening was suppressed at the site of damage (p. 16, [0116], lines 1-2). Therefore, Katzuo et al discloses a method comprising accumulation of the carrier at a damage site in a blood vessel and allowing the drug to act on the damaged site, as claimed in claims 17-21.

Overall, the prior art of Katzuo et al explicitly or inherently discloses all the properties of the claimed invention. Therefore, Katzuo et al anticipates the instant claims.

8. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCIA S. NOBLE whose telephone number is (571)272-5545. The examiner can normally be reached on M-F 9 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch, Ph.D./
Primary Examiner, Art Unit 1632

Marcia S. Noble
AU 1632